62 Effects of Smoking on Benzo (α) pyrene and Glutathione Metabolizing Enzymes in Man

Christel Bluhm

Department of Dermatology, Heinrich-Heine-University, Moorenstr. 5, D-4000 Düsseldorf, FRG

Smoking is the most important cause of lung cancer. We studied the influence of smoking habits on the metabolism of benzo (α) pyrene and glutathione in 190 patients with primary bronchial carcinoma. Seventy-two percent of these patients were current smokers, 18 % were former smokers, and 10 % were lifelong nonsmokers.

Benzo (α) pyrene (BP), like other polycyclic aromatic hydrocarbons (PAHs), needs activation to reactive metabolites to bind to cellular macromolecules and to exert adverse effects. Detoxification is preferably by conjugation with glutathione.

There were no significant differences in the activities of BP metabolizing enzymes in the lung tissue of smokers, former smokers, and nonsmokers. Only a tendency to slightly higher monooxygenase activities in smokers indicated an induction of these enzyme system to generate reactive metabolites. Glutathione and related enzyme activities showed a positive correlation to the number of cigarettes smoked daily. In contrast, the number of pack years and the duration of nicotine abuse had no effect either on PAH or glutathione metabolism.

These data indicate that the adverse effects of smoking may be based on a slight increase in the activity of cytochrome P450-dependent monooxygenases thus initiating the activation of BP to reactive metabolites. The correlation of the number of cigarettes smoked with the activities of the enzymes involved in detoxification is in favor of an increased requirement to remove reactive metabolites from the cell to prevent accumulation of toxic compounds. Thus detoxification in smokers has to be more effective than in nonsmokers to prevent early malignant transformation. As soon as detoxification becomes less effective due to an impairment of cellular defense mechanisms with age, an excess of nicotine abuse or other factors, a disturbance in the delicate balance between the generation and detoxification of reactive metabolites may result. This will facilitate tumor development.